

### **REMARKS**

In the Office Action mailed July 13, 2005, Claims 1-33 were pending for consideration. All of the claims were objected to and rejected on various statutory grounds, each of which is addressed in turn below.

By the present amendment, Claims 3, 5, and 11 have been amended to correct typographical errors. Applicants respectfully submit that no new matter is added thereby. Additionally, Claim 19 has been amended in a manner as suggested by the Examiner during the interview of September 12, 2005. Furthermore, Claims 3-11 have been amended as outlined below. Support for these amendments can be found on page 13 lines 9-28. Also, Claims 34-36 have been added. Support for these claims can be found on page 11, lines 15-16, and page 20, lines 2-4. Applicants submit that no new matter has been added thereby.

The specification has also been amended to correct the priority of the application, as well as to correct various objections noted by the Examiner.

It is to be understood that all amendments have been made solely for the purpose of expediting prosecution of the present application, and without conceding the correctness of the Examiner's rejection. Accordingly, Claims 1-33 remain pending in the present application. Applicants respectfully submit that the present claims are allowable over the Patel reference, and that the rejections in view thereof are now moot.

#### **Claim and Specification Objections:**

Claim 3 was objected to because of a misspelling of the word "fatty," which has been amended to the correct spelling.

Claims 5 and 11 were objected to because of a misspelling of the word "nicotinate."  
Both claims have been amended to the correct spelling.

Claim 7 was objected to for lacking antecedent basis for the term “the ester.” This claim has been amended to correct the dependency of Claim 7 to Claim 6.

The Applicants have noted the numerous objections to the specification regarding the use of trademarks, and the minor informalities listed as (i) – (iii). Numerous trademarks have been amended to all-caps, and the minor informalities have been corrected.

35 U.S.C. 112, Second Paragraph Rejections:

Claims 13-15, 17-19, and 30 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite due to the use of the term “about” in connection with the recited numerical ranges. During the interview of September 12, 2005, the issue of the term “about” was discussed in terms of an entire range. The discussion pertained primarily to the use of the term “between about.” It was agreed that the Examiner would withdraw the 35 U.S.C. § 112 rejections if the word “between” was deleted. As such, Claim 19 has been amended accordingly. Regarding Claims 13-15, 17-18, and 30, Applicants note that MPEP § 2173.05(b) addresses use of the term “about” and states that the use thereof has been held to be definite with respect to numerical ranges such as those in the present claims. It is generally accepted that this recitation provides flexibility to a numerical range endpoint by providing that room for a given value to be “a little above” or “a little below” the endpoint. As such, the Applicants respectfully request that these rejections be withdrawn.

Claims 3, 7-10, and 12 were rejected under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter that the Applicants regard as their invention. Specifically, the Examiner has alleged that the term “derivative” is a relative term that renders the claims indefinite. The Applicants respectfully disagree with the Examiner’s assertion. However, for the purpose of advancing prosecution in

the present application, and without conceding the correctness of the Examiner's position, Claims 3-6 and 8-11 have been amended to recited various specific derivatives of each stated compound. Reconsideration is therefore respectfully requested.

Claims 8-12 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite due to the use of the terms "slowly" and "high." The Applicants believe that the terms "slowly dissolving salt complex" and "high molecular weight" are common terms to one of ordinary skill in the art, and would thus be readily understood. In order to advance the prosecution of the present application, however, the terms "slowly" and "high molecular weight" have been deleted from claims 8 and 10 respectively. Reconsideration is requested.

Claim 8 was rejected under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter that the Applicants regard as their invention. Specifically, it is the Examiner's position that the term "insoluble carrier" is a relative term that renders the claims indefinite. The Applicant's respectfully disagree with this assertion. Claim 8 contains the limitation that the release modulator may include, *inter alia*, an insoluble carrier. The term "insoluble carrier" should not be considered in a vacuum, but in relation to the term "release modulator." A release modulator merely modulates the release of the drug being administered. Any range of insolubility that modulates such administration would be considered to be within the claim scope. Once in possession of the present disclosure, one of ordinary skill in the art would readily understand be able to formulate an insoluble carrier for a given active agent that would provide modulation of release without undue experimentation. It was not the Applicants' intent to provide an exact range of acceptable insolubilities because variation of such provides a variation in the modulation of the release of the drug, and such insolubility variation would be understood by one of ordinary skill in the art. The Applicants respectfully remind the

Examiner that it is not the public at large that needs to be informed of the boundaries of the claims, but one of ordinary skill in the art. In addition to understanding the basic principle of release modulation by an insoluble carrier, one of ordinary skill in the art would be further informed as to the nature of insoluble carriers through the examples provided. Accordingly, the Applicants respectfully request reconsideration of this rejection.

Claims 21-23 were rejected under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter that the Applicants regard as their invention. Specifically, it is the Examiner's position that the term "correlation coefficient" is a term that renders the claims indefinite because the specification lacks a specific mathematical definition of how such a coefficient is to be calculated. The Applicants assert, however, that one of ordinary skill in the art would be familiar with, and have the knowledge to readily calculate a correlation coefficient. As evidence of such, page 183 of Principles of Procedures of Statistics (hereinafter "Steel") is hereby submitted as Exhibit 1. Steel describes the correlation coefficient defined by equation 10.1, and provides sufficient detail that it may be readily calculated. Accordingly, it is the Applicants' position that such calculation is well within the knowledge of one of ordinary skill in the art, and as such, respectfully requests that the rejections be withdrawn.

Obviousness-Type Double Patenting Rejections:

The Examiner has rejected claims 1-33 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the composition claims of U.S. Patent Nos. 6,267,985; 6,294,192; 6,309,663; 6,383,471; 6,451,339; 6,458,383; 6,468,559; 6,569,463; 6,720,001; and 6,761,903; and are provisionally rejected over the composition claims of U.S. Patent Application Nos. 09/716,029; 10/074,687; 10/159,601; 10/322,344; 10/397,969;

10/428,431; 10/444,935; 10/700,838; and 11/031,527. Terminal disclaimers are filed herewith in order to expedite the present prosecution, without agreeing to the Examiner's assertions.

35 U.S.C. § 102 Rejections:

The Examiner has rejected Claims 1-26 and 28-33 under 35 U.S.C. § 102(a) or 35 U.S.C. § 102(e) as being allegedly anticipated by U.S. Pat. No. 6,569,463 (hereinafter "Patel"). By the present amendment, the specification has been amended to correct the priority of the present application, as was discussed with the Examiner during the interview of September 12, 2005. As such, the present application now derives benefit from the Patel patent. Thus the Applicants respectfully assert that Patel is not available as a prior art reference against the present application, and these rejections have been rendered moot.

35 U.S.C. § 103 Rejections:

The Examiner has rejected Claims 1-33 under 35 U.S.C. § 103(a) as being allegedly unpatentable over Patel in view of U.S. Patent No. 5,403,593 (hereinafter "Royce"), U.S. Patent No. 6,458,373 (hereinafter "Lambert"), U.S. Patent No. 2,680,749 (hereinafter "Cawley"), U.S. Patent No. 6,623,755 (hereinafter "Chen"), The Merck Index (Monograph 1882), "Ventricular Fibrillation, an Uncontrolled Arrhythmia Seeking New Targets" (hereinafter "Beatch"), and "A Primer of Drug Action" (hereinafter "Julien"). As has been discussed above, the present application as amended derives benefit from the Patel patent, and thus Patel is not available as a prior art reference to use in establishing a *prima facie* case of obviousness. Without Patel, the remaining references do not provide the requisite teaching or suggestion to establish such a *prima facie* case.

Accordingly, Claims 1-33 remain pending in the present application. In view of the discussion during the Examiner interview of September 12, 2005, Applicants respectfully submit

that the present claims are allowable over the Patel reference, as discussed, and that the rejections in view thereof are now moot.

**CONCLUSION**

In view of the foregoing, the Applicants believe that Claims 1-33 present allowable subject matter and the prompt allowance thereof is requested. If any impediment to the allowance of these claims remains after consideration of the present amendment and above remarks, and such impediment could be removed during a telephone interview, the Examiner is invited to telephone the undersigned attorney, so that such issues may be resolved as expeditiously as possible.

Please charge any additional fees except for Issue Fee or credit any overpayment to Deposit Account No. 20-0100.

Dated this 13<sup>th</sup> day of January, 2006.

Respectfully submitted,

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Exhibit A

# Principles and Procedures of STATISTICS

WITH SPECIAL REFERENCE TO  
THE BIOLOGICAL SCIENCES

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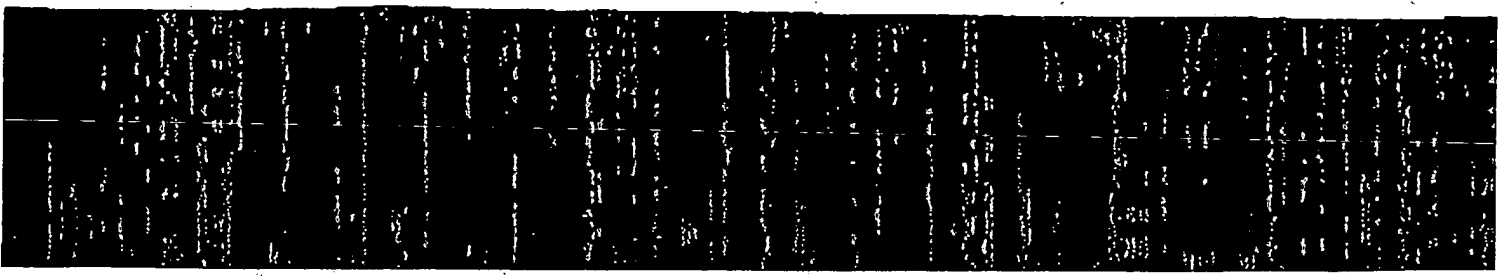
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PRINCIPLES AND PROCEDURES OF STATISTICS

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*Math. Stat.*, 10: 162-186 (1939).  
 umbridge University Press, 1951.  
 ied to biological assays," *J. Roy. Stat.*

*Biometrics Bull.*, 2: 101-109 (1946).

## Chapter 10

### LINEAR CORRELATION

**10.1 Introduction.** Bivariate distributions were discussed briefly in Sec. 9.12. In sampling from a bivariate population, an observation consists of a random pair of measurements. Here, two regressions are possible and valid although, ordinarily, only one regression is desired. A summary of the data in a sample from a bivariate distribution consists of two means, two variances, and the covariance. The covariance may be replaced without loss of information by the coefficient of determination or its square root, the coefficient of linear correlation. This chapter deals with linear correlation.

**10.2 Correlation and the correlation coefficient.** Correlation, like covariance, is a measure of the degree to which variables vary together or a measure of the intensity of association. As such, it must be symmetric in the two variables. The sample linear correlation coefficient, also called the simple correlation, the total correlation and the product-moment correlation, is used for descriptive purposes and is defined by Eq. (10.1).

$$r = \frac{\Sigma(X - \bar{x})(Y - \bar{y})/(n-1)}{\sqrt{\Sigma(X - \bar{x})^2/(n-1)}\sqrt{\Sigma(Y - \bar{y})^2/(n-1)}} \\ = \frac{\Sigma(X - \bar{x})(Y - \bar{y})}{\sqrt{\Sigma(X - \bar{x})^2}\sqrt{\Sigma(Y - \bar{y})^2}} = \frac{\Sigma xy}{\sqrt{\Sigma x^2}\sqrt{\Sigma y^2}} \quad (10.1)$$

It is assumed that, in the population, a linear relation exists between the variables. This is a valid assumption when sampling is from a bivariate normal distribution. The correlation coefficient  $r$  is an unbiased estimate of the corresponding population correlation coefficient  $\rho$  (Greek rho) only when the population parameter  $\rho$  is zero. Unlike a variance or a regression coefficient, the correlation coefficient is independent of the units of measurement; it is an absolute or dimensionless quantity. The use of  $X$  and  $Y$  is no longer intended to imply an independent and a dependent variable.

Some insight for the interpretation of linear correlation may be gained from the scatter diagrams of Fig. 10.1 for which the data have been especially manufactured. In part i of the figure, the points cluster about a line through  $(\bar{x}, \bar{y})$  and parallel to the  $X$  axis simply because the variance of  $X$  is larger than that of  $Y$ . The lack of a tendency to cluster about any line other than one through  $(\bar{x}, \bar{y})$  and parallel to an axis is typical of data where there is little or no linear correlation. In such cases, each regression line is close to a line through  $(\bar{x}, \bar{y})$

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